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(54) Title: **TAK1-MEDIATED INHIBITION OF OSTEOGENESIS**

(57) Abstract: This invention is directed to methods, nucleic acids and compositions in TAK1-mediated regulation of SMAD activity. Promotion of TAK1 interaction with MH2 domains in SMADs negatively regulates SMAD biological activity. BMP-mediated SMAD activity is subject to TAK1 effects.



WO 2004/087862 A3

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PCT/IL04/00286

A. CLASSIFICATION OF SUBJECT MATTER

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US CL : 536/23.1; 435/325; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/23.1; 435/325; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SHIBUYA et al. Role of TAK1 and TAB1 in BMP signaling in early Xenopus development. EMBO J. February 1998, Vol. 17, No. 4, pages 1019-1028, see entire document	2,3,6-10
Y		1,4,5,11-86
Y	MOCHIDA et al. ASK1 Inhibits Interleukin-1 induced NF-KB Activity through Disruption of TRAF6-TAK1 Interaction. J. Biol. Chem. October 2000. Vol. 275, No. 42, pages 32747-32752, see entire document	1,14,19,20,41,42
Y	YOSHIDA et al. Negative Regulation of BMP/SMAD Signaling by Tob in Osteoblasts. Cell. December 2000. Vol. 103, pages 1085-1097, see entire document	18,24,25,27-30,35-40,47-56,058-75,78-81
Y	CARNINCI et al. Normalization and Subtraction of Cap-Trapper-selected cDNAs to prepare Full-Length cDNA Libraries for Rapid Discovery of New Genes. Genome Res. October 2000. Vol. 10, pages 1617-1630, see entire document.	4,5,10-12,15,16,22,23,34,45,57,69,70,76,82-86
Y	YAMAGUCHI et al. Identification of a member of the MAPKKK Family as a potential Mediator of TGF-beta signal transduction. Science. December 1995. Vol. 270. pages 2008-2011, see entire document	4,5,10-12,15,16,22,23,34,45,57,69,70,76,82-86

☒ Further documents are listed in the continuation of Box C.



See patent family annex.

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International application No.
PCT/IL04/00286

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HOFFMAN et al. TGF-Beta-activated kinase-1 (TAK1), a MAP3K, interacts with SMAD proteins and interferes with osteogenesis in murine mesenchymal progenitors. J. Biol. Chem. May 2005. M5033682000, pages 1-33, see entire document	1-86

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:

EAST, STN: FILE MEDLINE

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